

# The Scientific Contributions of Paul D. MacLean (1913–2007)

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**Abstract:** Paul D. MacLean, a leading brain scientist of the 20th century, died on December 26, 2007. We review his life as a scientist and highlight some of his most important research contributions.

**Key Words:** Limbic system, triune brain.

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December 26, 2007 marked the passing of Paul D. MacLean one of the leading brain scientists of the 20th century and a long-time member of this Journal's Editorial Board (Fig. 1). In a remarkably long and productive career, he established the parameters for investigating the evolution and functioning of the emotional brain and set the stage for current research in affective and social neurosciences. He is best known for identifying and naming the limbic system in 1952, but this was only the beginning of his research contributions. In 1990, nearly 40 years later, he summarized his lifetime of research in his magnum opus, *The Triune Brain in Evolution* (MacLean, 1990; hereafter "TB"). There he discussed the ramifications of the limbic system concept and his subsequent findings on brain evolution and behavior culminating in his proposal of a new brain model he called "the Triune Brain." His research has altered our view of *Homo sapiens* and our understanding of brain evolution and behavior. Words cannot capture Paul MacLean's elegance as a scientist, compassion as a human being and his impact in inspiring others. Those who spent time with him appreciated these qualities.

## MacLean's Work in Historical Perspective

MacLean's contributions have impacted evolutionary biology, neuroethology, clinical neuroscience, neurology, psychiatry, and the social sciences. He posed 2 critical research questions that are pertinent to each of these fields: (1) "where do subjective emotional experiences reside in the brain?" and (2) "is the functional circuitry of the brain inherited in the evolution of vertebrates and, if so, how did these circuits evolve?" He was particularly interested in the evolution of the family, writing "the evolution of the limbic system is the history of the evolution of mammals, whereas the history of the evolution of mammals is the history of the evolution of the family (TB, p. 247)."

MacLean helped establish an approach to neuroscience essentially unknown in the United States at the time he began his research. In Europe, the field of neuroethology had arisen with

primary focus on nonmammalian models. Still, in Zurich, Switzerland, W. R. Hess and his coworkers, using electrical brain stimulation of indwelling electrodes in cats, were mapping out areas in the hypothalamus and other parts of the diencephalon from which coordinated species-typical aggressive and fear-like behavior could be elicited. MacLean visited the Zurich laboratory in 1956, but did not refer to the work that came out of that laboratory in his own publications. Subsequently, with Detlev Ploog, he developed a laboratory environment where species-typical behavior could be studied in a primate, the squirrel monkey (MacLean, 1962). Ploog set up his own laboratory, the Department of Primate Behavior, at the Max Planck Institute for Psychiatry in Munich. There, he focused in large measure on squirrel monkey vocal behavior and its underlying mechanisms (e.g., Ploog, et al., 1975). MacLean returned to the United States initiating his own research on brain and behavior. His approach was clearly ethological and he emphasized the importance of preparing an ethogram, an inventory of the behavior of a species that thoroughly describes its behaviors and organizes them into categories. He was particularly interested in identifying behavioral master routines and subroutines. Although he never used the term 'neuroethology,' MacLean was clearly an important early pioneer in this field.

## Limbic System

MacLean was aware of Paul Broca's (Broca, 1878) observation that the 'limbic lobe,' so named because it surrounds the brainstem, is common to the brains of all mammals. He was intrigued with James Papez's (Papez, 1937) proposal that emotional experience is based on connections linking the hypothalamus with the limbic lobe (MacLean, 1993) and visited Papez to discuss his observations with neurological patients. MacLean's curiosity about subjective emotional experience arose from his earlier work with people with psycho-motor epilepsy whose symptoms included emotional feelings and viscerosomatic symptoms (MacLean, 1949). Seeking to account for sensations involved in the visual, olfactory, and auditory auras associated with these seizures, he reasoned that the external sensory apparatus must have access to the brain circuits where seizures arose and that cortical association pathways could potentially connect visual, auditory, and somatic neocortical areas with the hippocampal gyrus. MacLean amplified and reconceptualized Papez's proposal and suggested that a circuit consisting of the limbic lobe and its major connections in the forebrain—the hypothalamus, amygdala, and septum—constituted a "visceral brain" (MacLean, 1949). Seeking greater clarity, he introduced the term "limbic system" (MacLean, 1952) soon afterward. He wrote that emotional feelings elude "the grasp of the intellect" (MacLean, 1949 p. 348) because their origins lie in evolutionary primitive structures preventing their communication in verbal terms. He wrote that this underlying neurobiology provides a clue to understanding the difference between what we feel and what we know (MacLean, 1993). His research focus on the limbic system led to the establishment of the Section on Limbic Integration and Behavior at the National Institute of Mental Health (NIMH). Subsequently, with the creation of the new NIMH Laboratory of Brain Evolution and Behavior on a rural farm owned by the NIH near Poolesville, Maryland, MacLean, as laboratory chief, expanded his research. There he studied brain mechanisms underlying behavior in animal models under semi-natural conditions.

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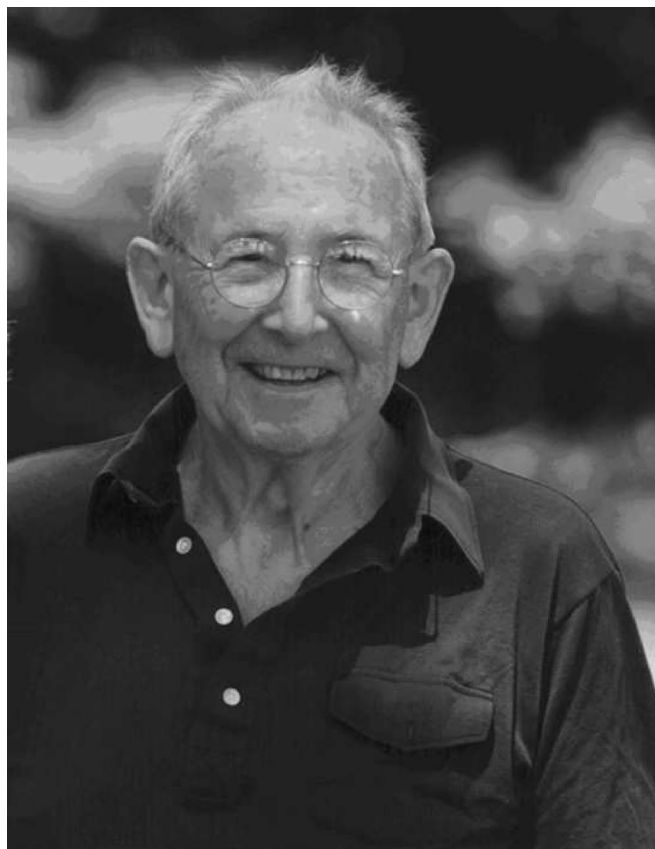


FIGURE 1. Paul D. MacLean. Photo by Alex MacLean.

### Triune Brain

At the Laboratory of Brain Evolution and Behavior, MacLean embarked on a series of experiments on the effects of targeted brain lesions on species-typical behavior in lizards (Greenberg, et al., 1979), and squirrel monkeys (MacLean, 1978), and the role of limbic cortex on play and maternal behavior in hamsters (Murphy, et al., 1981). These studies resulted in his triune brain proposal first fully enunciated in his Hinck's Memorial Lecture in 1969 (MacLean, 1973). Tracing brain evolution from reptiles to mammals, he established that the reptilian forebrain, characterized by greatly enlarged basal ganglia, resembles the striatopallidal complex of mammals. Later, describing forebrain structures in an evolutionary context, MacLean coined the term "protoreptilian formation," or "R-complex," in describing the striatal complex, locating it at the base of the forebrain in reptiles, birds, and mammals (TB, p. 15). In the triune brain model he reconceptualized the limbic system as the "paleomammalian brain."

In enunciating his triune brain proposal from an evolutionary perspective, MacLean wrote (1967, p. 375): "There are those who argue that one has no right to apply behavioral observations on animals to human affairs, but they may be reminded that man has inherited the basic structure and organization of 3 brains, 2 of which are quite similar to those of animals. They evolved somewhat like a house to which wings and superstructure are added. Despite their great disparity in structure and chemistry, all 3 must function together. Man's brain of oldest heritage is basically reptilian. It forms the matrix of the brain stem and comprises much of the so-called reticular system, midbrain, and basal ganglia. Superimposed on the reptilian is a structure inherited from lower mammals.

It consists of the 2 oldest forms of cerebral cortex together with related nuclei of the brain stem. As it is common to the brains of all mammals, 1 might refer to it as the paleomammalian brain [limbic brain]. Superimposed on the old mammalian brain and appearing late in evolution is a more elaborate form of cortex called neocortex which, together with its associated nuclei of the brain stem, reaches the most advanced stage of development in man and overshadows the rest of the brain. It can be characterized as neomammalian in structure and organization." Accompanying this text is the now-famous figure (Fig. 2), showing in schematic side view the 3 basic types of brains that MacLean proposed as man's inheritance.

### The Family and the Brain

MacLean's appreciation of the importance of family-related behavior in the evolution of the mammalian brain became a major theme in his later writings. He summarized this research in his Adolph Meyer lecture to the American Psychiatric Association in Toronto, Canada in 1982 (MacLean, 1985). MacLean cited evidence that the thalamo-cingulate division of the limbic system was unique to mammals, hence it followed that this structure would mediate behaviors that were either unique to mammals, or, at the very least, largely absent in infra-mammalian vertebrates. These behaviors included play, nursing and maternal care, and audiovocal mother-infant communication (the separation or isolation cry). Two classic papers examined his hypotheses about the brain and family life. One (Murphy, et al., 1981) showed that hamsters deprived from birth of their neocortex, but sparing limbic cortex, retained both playfulness when young and maternal care as adults, but that play was disrupted if the limbic cortex was damaged. A later study (MacLean and Newman, 1988), involving lesions placed in midline frontolimbic cortex of adult squirrel monkeys, showed that such lesions largely eliminated production of the adult form of the "isolation peep," which in infants serves as the species-specific infant cry.

### MacLean's Views on Medical Education and the Future of Psychiatry

MacLean spoke widely about the implication of brain evolution and behavior, addressing educators on the importance of providing an education that took into account the evolution of our

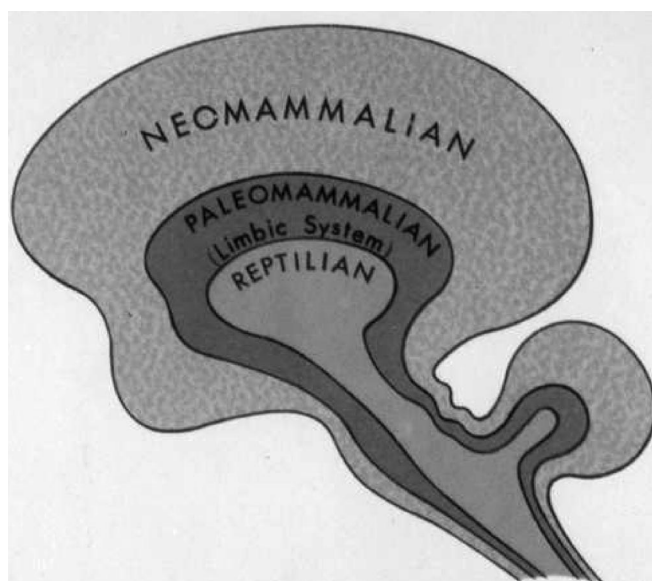


FIGURE 2. From the frontispiece to MacLean, 1990.

species). He expressed concern that the present emphasis in psychiatry on finding a chemical cure for every condition could lead to patients being “manipulated like machines.” As an antidote to this, he proposed an *evolutionary psychiatry* (MacLean, 1985) whose domain is the subjective self. He proposed that “evolutionary psychiatry will focus on the integrated function of the still evolving brain (MacLean, 1985).” MacLean emphasized the importance of empathy as a mark of integrated brain functioning in brain evolution (Harris, 2003). MacLean concluded a paper on the evolution of audiovocal communication on an optimistic note (MacLean, 1988): “Judged by human behavior, it was as though there were a directed evolution towards the development of a concern not only for the feelings and future welfare of human beings, but also for all living things.”

## CONCLUSIONS

It remains to be seen the extent to which MacLean’s work will continue to stimulate further research and if his ideas will be put into practice. It was his hope that a national “brain library” be established to facilitate comparative study. Such a library has come into being (<http://nmhm.washingtondc.museum/collections/neuro/neuro.html>). It is ironic however, that MacLean’s own extensive collection of brain histology is not part of the museum’s collections, having been discarded during the last days before closing of his laboratory at the NIH Animal Center (R. Gelhard, personal communication).

Several symposia have been held to honor MacLean. One, held in Boston in 1999, resulted in an edited volume of papers whose contributors were familiar with MacLean’s work (Cory and Gardner, 2002). Subsequently, a special satellite symposium to the International Behavioral Neuroscience Society’s annual meeting held in Capri, Italy was devoted to MacLean. This led to a special issue of *Physiology and Behavior* with papers from attendees, along with additional invited contributions. The preface to that issue (Lambert and Gerlai, 2003) contained a fitting expression of appreciation to MacLean and his work: “A special thanks is extended to this amazing scientist for opening the door to social and evolutionary neuroscience so that today’s scientists and practitioners can embark on many paths to understand more about the brain in its natural context” (p. 342).

A collection of MacLean’s papers and correspondence is available at the National Library of Medicine in Bethesda, MD. A finding aid to the collection is available at <http://nlm.nih.gov/hmd/manuscripts/ead/maclean534.html>.

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